

Table 1: HEPARANASE SEQUENCE HOMOLOGY DATA

	10	20	30	40	50	60
mouse	-MLR-----	LLLILWGPGLGALAAQGAPAGTAPTDVVDEFYTKRPLRSVSPSFLSIT				
rat	-MLRP-----	LLLILWGRIRALTQGTPAGTAPTKDWDLEFYTKRLFQSVPSPFLSIT				
human	MLLRSKPALPPPIMLLLIGPGLPSPGALPRPAQAOQDVVDLDFTQEPHLVSPSPFLSIT					
chicken	-MLVLLLVLVLLAVPP-----	RR-TAELQLGLREPIGAVSPAFLSLT				
	***: * * : *: * : .. : ***: ***: *				
	70	80	90	100	110	120
mouse	IDASLATDPRLTFLGSPRLRALARGLSPAYLRFGGTKTDFLIFDPDKEPTS	EERSYWK	S			
rat	IDASLATDPRLTFLGSPRLRALARGLSPAYLRFGGTKTDFLIFDPDKEPTS	EERSYWQS				
human	IDANLATDPRLTFLGSPKLRLTARGLSPAYLRFGGTKTDFLIFDPKKESTFEERSYWQS					
chicken	LDASLARDPRLPVALLRHPKLIHTLASGLSGFLRFGGTSTDFLIFPNPKDSTWEEKVLSEF					
	:***: ***: * : * : * ; ***: ***: ***: ***: * : * : * :					
	130	140	150	160	170	180
mouse	QVNHDICRSEPVSAAVLRLKLOVEPFQELLLLIREQYKEFKNSTSRSVDMLYSFAC	KCS				
rat	QDNNDICGSESVSADVLRLKLOMEUPFQELLLLIREQYQREFKNSTSRSVDMLYSFAC	KCS				
human	QVNQDICCKYGSIPPDVEEKRLRELPYQEQLLLREHYOKKFKNSTSRSVDMLYTFAC	S				
chicken	QAK-DVCEAWPSFAVVP[LLTQPLQEKLLIAEWSKKHNTITTRSTLDILHTPASSS					
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	190	200	210	220	230	240
mouse	GLDLIFGLNALLRTPDLRWNSNAQQLLDYCSSKGYNISWELGNEPNSFWKKAHILIDGL					
rat	RLDLIFGLNALLRTPDLRWNSNAQQLLDYCSSKGYNISWELGNEPNSFWKKAQISIDGL					
human	GLDLIFGLNALLRTPDLRWNSNAQQLLDYCSSKGYNISWELGNEPNSFLKKADIFINGS					
chicken	GFRLVFGNLALLRRAGLQWDSSNAKQLLGCAQRSYNISWELGNEPNSFRKKSGICIDGF					
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	250	260	270	280	290	300
mouse	OLGEDFVELHKL[QKS-AFONAKLYGPDIGQPRGKTVKLRLSFLKAGGEVIDSLTWHHYY					
rat	OLGEDFVELHKL[QKS-AFONAKLYGPDIGQPRGKTVKLRLSFLKAGGEVIDSLTWHHYY					
human	OLGEDYIQLHKL[LRKS-TFNAKLYGPDVGQPRRKTAKMLKSLFKAGGEVIDSVTWHHYY					
chicken	QLGRDFVHLRQL[SQHPLYIHAELYGLDVQPRKHTQHLLRSFMKSGGAIDSVTWHHYY					
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	310	320	330	340	350	360
mouse	LNGRIATKEDFLSDALDTFILSVQKILKVTKEITPGKVKWLGETSSAYGGAPLLSNTF					
rat	LNGRVATKEDFLSSDVLDTFILSVQKILKVTKEITPGKVKWLGETSSAYGGAPLLSNTF					
human	LNGRTATREDFLNPVDLTDIPISSVQKVQQVVESTRPGKVKWLGETSSAYGGAPLLSDTF					
chicken	VNGRSATREDFLSPEVLDSTATAIHDLGIATEATVPGKVKWLGETGSAYGGAPQLSNTY					
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	370	380	390	400	410	420
mouse	AAGFMWLDKLGLSAQMGIEVVMRQVFQAGNYHLVDENFEPLPDYWLSSLFKKLGVPRVL					
rat	AAGFMWLDKLGLSAQMGIEVVMRQVFQAGNYHLVDENFEPLPDYWLSSLFKKLGVPRVL					
human	AAGFMWLDKLGLSARMGIEVVMRQVFQAGNYHLVDENFDPLPDYWLSSLFKKLGVPRVL					
chicken	VAGFMWLDKLGLAARRGIDVVMRQVSFGAGSYHLVDAGPKLPLDYWLSSLKYKRLGVPRVL					
	*****: * : * : * : * : * : * : * : * : * : * : * : * : * : * : * : * :					
	430	440	450	460	470	480
mouse	LSRVKGPDRSKLRVYLHCTN[YHPRYQEGDLTLVVLNINHNVTKHLKVPPLFRKPVDTYL					
rat	MSRVKGPDRSKLRVYLHCTN[YHPRYREGDLTLVVLNINHNVTKHLKLEPPMFSRPVDTYL					
human	MASVQGSKRRLKRVYLHCTNDNPRYKEGDLTLVAININHNVTKYLRLPYPPFSNKQVDTYL					
chicken	QASVQADARPRVYLHCTPRHPKYREGDVTLFALNLSNVTQSLOLPQLWSKSVDQYL					
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	490	500	510	520	530	540
mouse	LKPSGPDGLLSKSVQLNGQILKMDVDEQTLPALTEKPLPAGSALSPLPAFSYGFFVIRNAKI					
rat	LKPFSGDGLLSKSVQLNGQILKMDVDEQTLPALTEKPLPAGSALSVPAPFSYGFFVIRNAKI					
human	LRLPLGPHGLLSKSVQLNGQILKMDVDDQTLPIMKPLPAGSSLSVPAPFSYGFFVIRNAKI					
chicken	LLPHGKDSILSRREVQLNGRILLQMVDDETLPALHEMALAPGSTLGLPAPFSYGFFVIRNAKI					
	***: * : * : * : * : * : * : * : * : * : * : * : * : * : * : * : * :					
mouse	AACI (SEQ ID NO:2)					
rat	AACI (SEQ ID NO:3)					
human	AACI (SEQ ID NO:4)					
chicken	IACI (SEQ ID NO:5)					

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Table 2- FUNCTIONAL PEPTIDE EPITOPE OF HEPARANASE

Peptide	Amino acid sequence	Location in SEQ ID NO 10	Property
p8 #7 SEQ ID NO:7	PAYLRFGGTKTDFLIFDPK	89-107	C-terminus of P8 - Dimerization
pep38 SEQ ID NO:6	CTNTDNPRYK	437-446	located 5 amino acids downstream of a heparin binding site
pep8 SEQ ID NO:8	SWELGNPNSFLKKA	219-233	contains the proton donor residue of the heparanase active site
pep9 SEQ ID NO:9	RPGKKVWLGETSSAY	334-348	contains the nucleophilic residue of the active site
Pep10 SEQ ID NO:10	TWHHYYLNGRTATR	294-307	Designed according to a 3D model as a surface exposed sequence, which bridges substrate binding and active site.

*NOTE: Specific peptide sequences are underlined in the sequence below

*NOTE: Mature heparanase dimer sequences in **bold face**:

MLLRSKPALPPPLMLLLGPLGPLSPGALPRPAQAQDVVDLDFFTQEPLH
LVSPSF**L**SVT**IDAN**L**ATD**PRF**L**ILL**GSP****KL**RTL**L**ARG**L**S**PAYLRFGGTKTD**
FLIFDPKKE**S**TEERSY**WQS**QVNQ**DICKY**GSI**PPDVEE**KLR**LEWPY**QEQL
LLREHY**Q**KKFKN**S**TYSRSSVDV**LYTF**FANCS**GLDL**IFGLN**ALLRT**ADI**QWN**
SSNAQ**LLD**YCSS**KGYNI**SWELGNPNS**FLKKAD**IFING**SQLGED**FIQLH
KLLRK**S**TFK**NAKLY**GPDVGQ**PRRK**TAKMLKS**FLKAGGE**VIDS**VTW**HHYYL**
NGRT**ATRED**FLNP**DVL**D**IFI**SSV**QKV**FQVV**E**STRPGKKV**WLGETSSAY****GG**
GAPL**LSDT**F**AAGFM**WLD**KLGLS**ARMGIE**VVMRQ**VFFGAG**NYHLV**DENFD**P**
LPDYW**LSLL**F**KKL**VGT**KVL**MASVQGS**KRR**KLV**Y**LHCTNTDNPRY**KEGDL**
TLYAI**NLHN**VTKY**LRL**PYP**FSNK**QVD**KYLLR**PLG**PHG**LLSK**SVQ**LNGL**T**
KMVDDQ**TL**PP**LM**EKPL**RPG**SSL**GLP**AF**SYS**FF**VIRNA****KV****A****CI** (SEQ ID NO:4)**

1/10

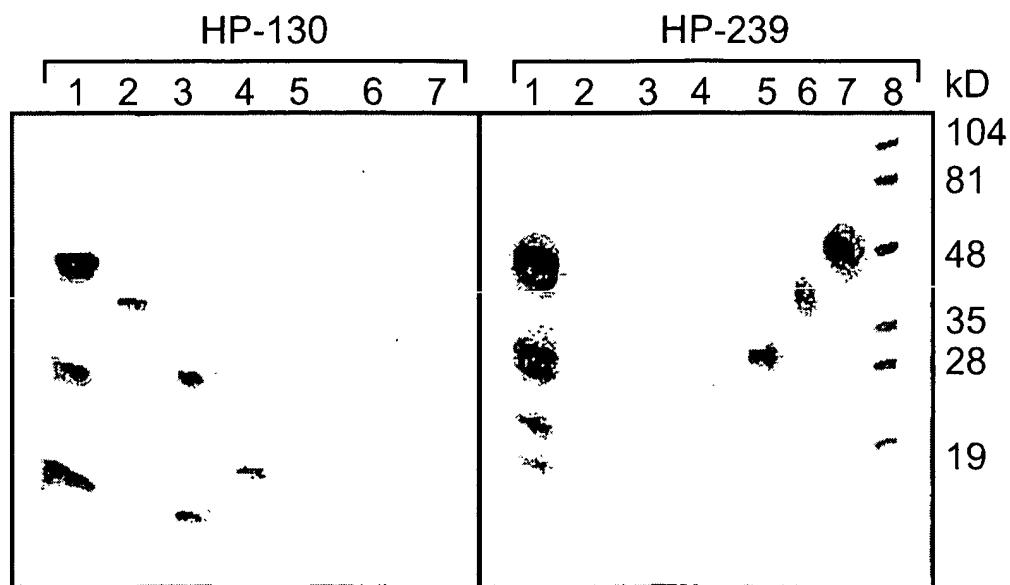


Fig. 1

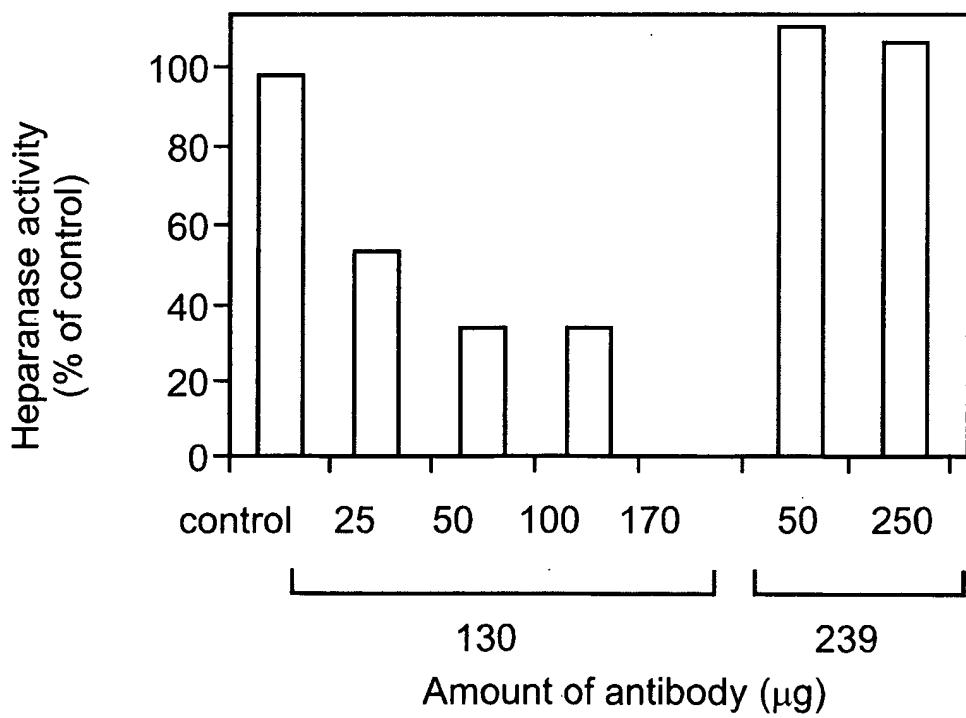


Fig. 2

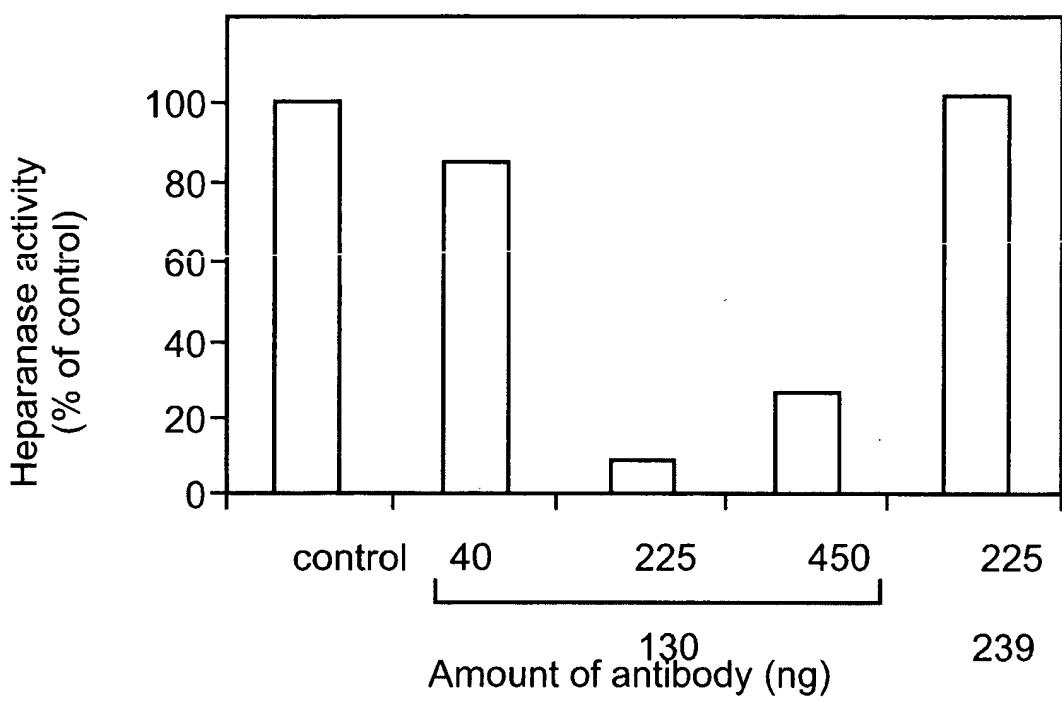


Fig. 3

Western blot analysis

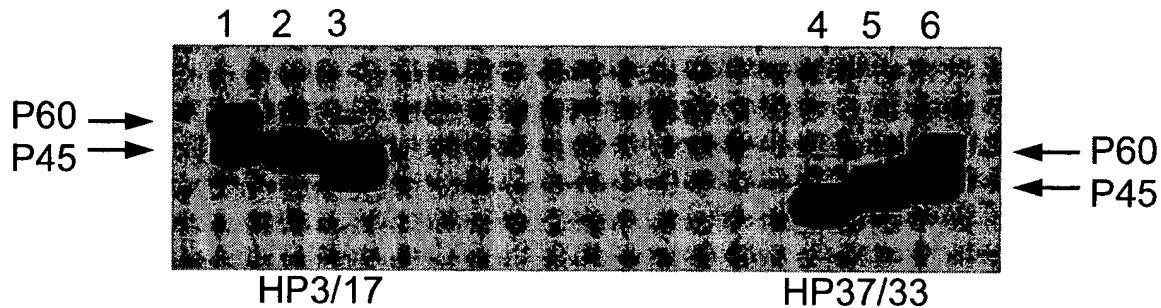


Fig. 4

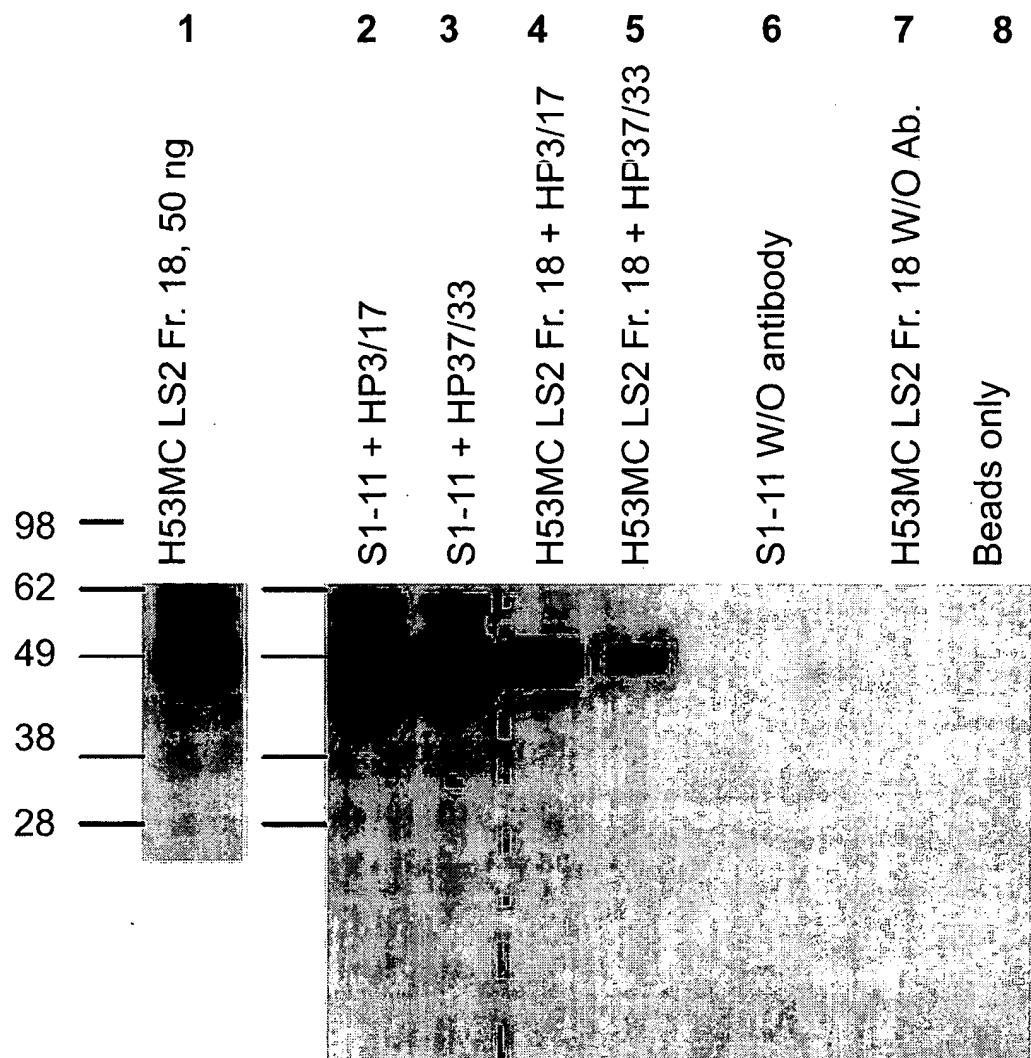


Fig. 5

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Fig. 6a

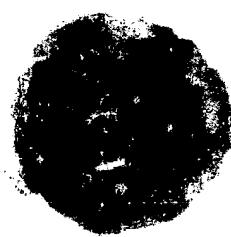


Fig. 6b



x 1000

HP37/33

Fig. 6c

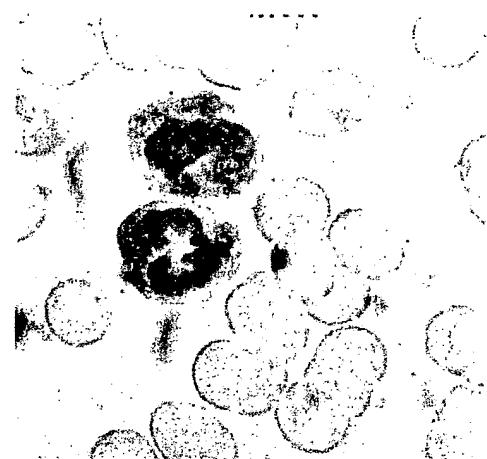


Fig. 6d

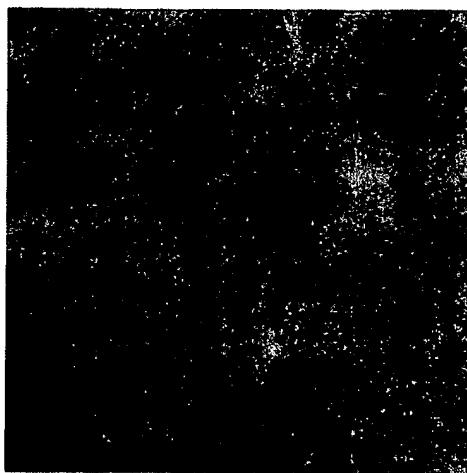


Fig. 7a

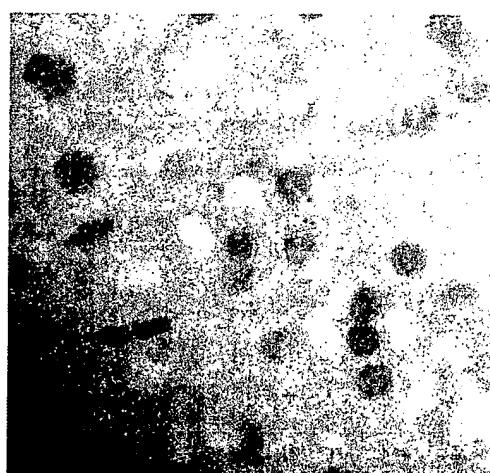


Fig. 7b

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Fig. 8a



Fig. 8b

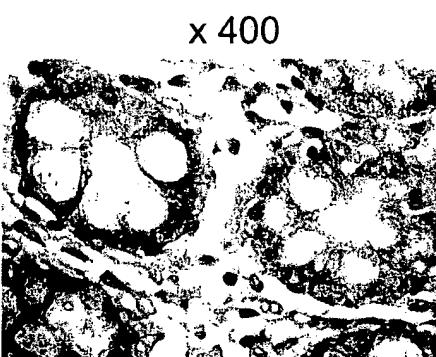
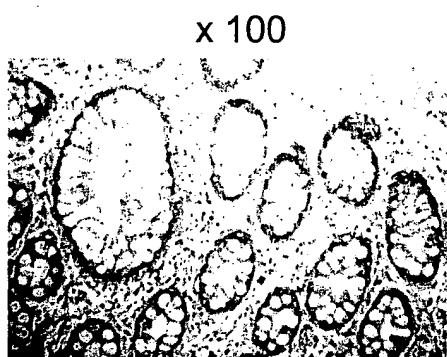


Fig. 9a

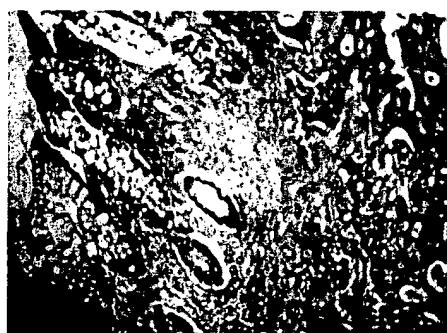


Fig. 9b

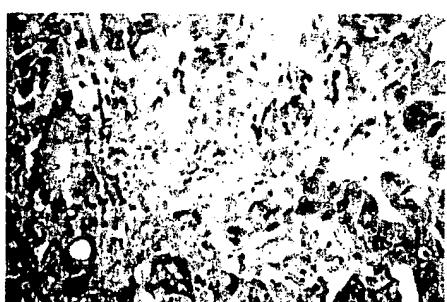


Fig. 9c

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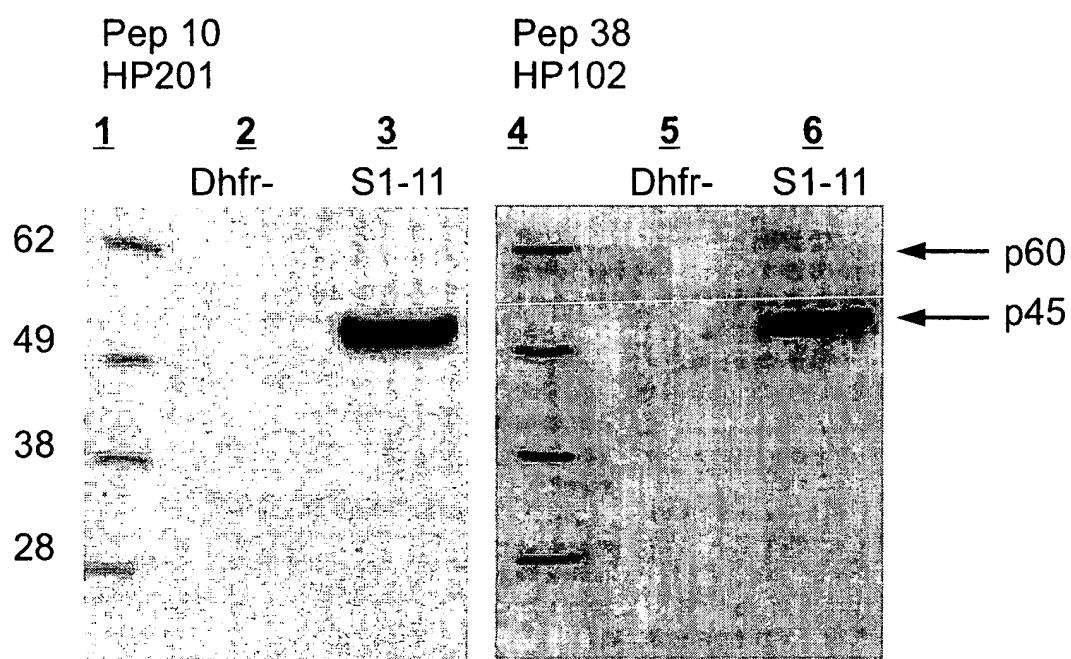


Fig. 10

Results

Group		Day 8	Day 12	Day 15	Day 18
A PBS	Mean	7.8	90.2	375.4	613.6
	SD	12.3	97.7	476.2	859.2
B HP130	Mean	0.0	34.2	188.4	298.2
	SD	0.0	42.8	165.6	111.7
C HP37/33	Mean	0.0	25.3	157.5	229.3
	SD	0.0	29.6	131.2	151.3

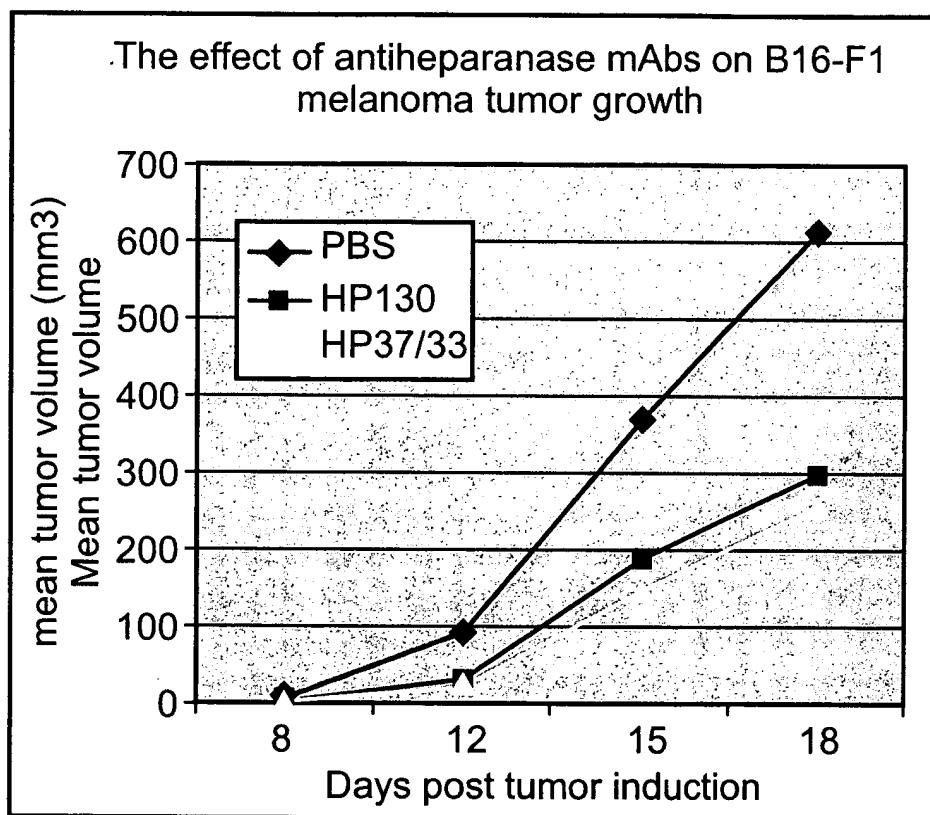


Fig. 11

Group	MEAN ARTHRITIC SCORE (4 legs)		
	Day 7	Day 11	Day 14
A-PBS	4.8	2.4	2.1
B-Mouse a human IgG3	4.9	3.4	2.5
C-HP3/17	4.2	2.1	1.5

Fig. 12

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The effect of HP3/17 on NOD mice survival

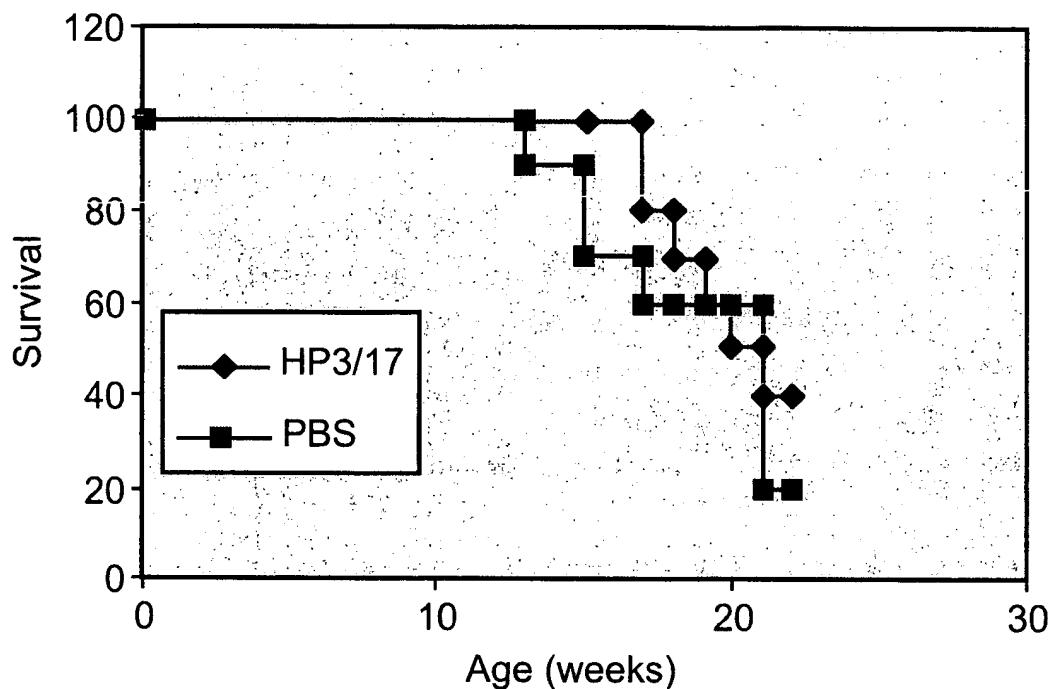


Fig. 13

HP37/33

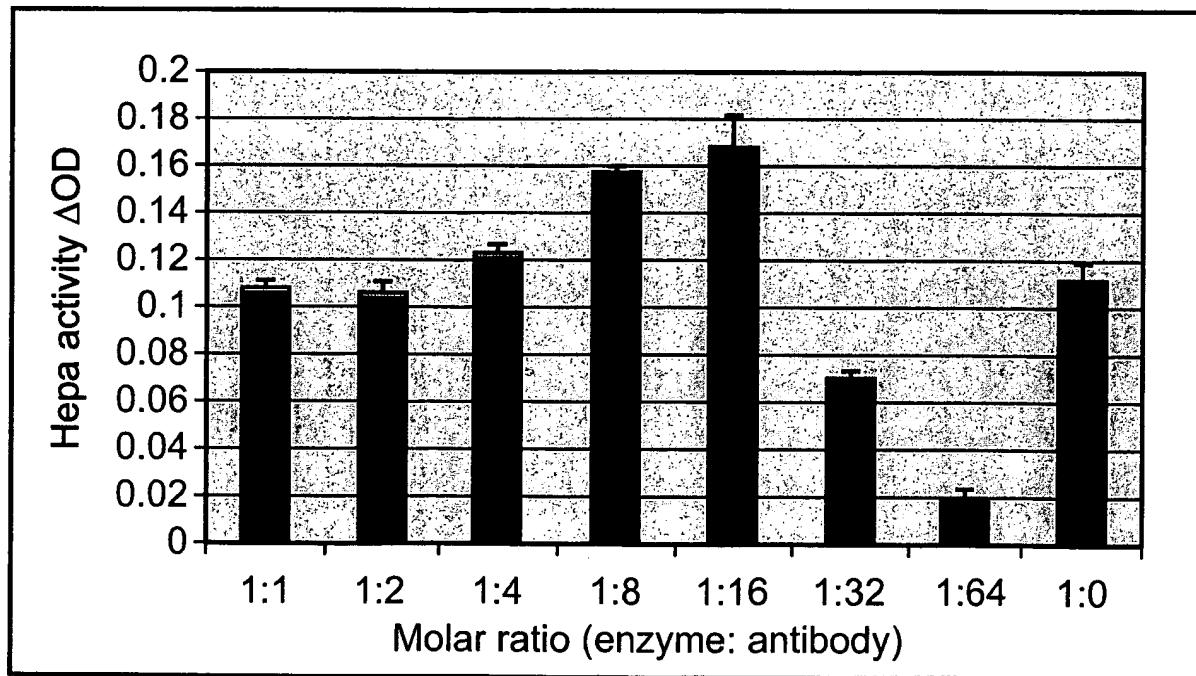


Fig. 14a

HP3/17

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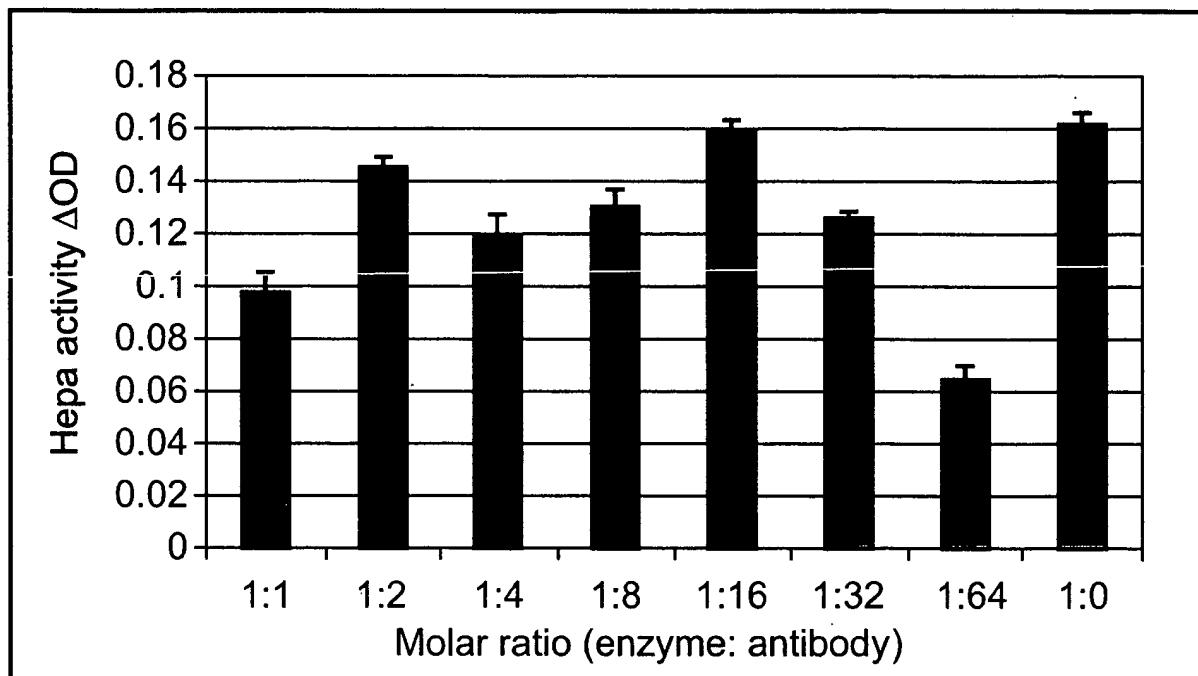
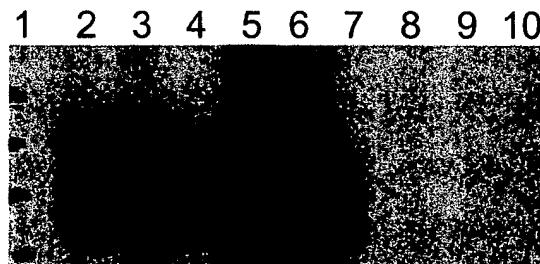


Fig. 14b

Epitope mapping

HP135.108

Fig. 15a



HP37/33

Fig. 15b

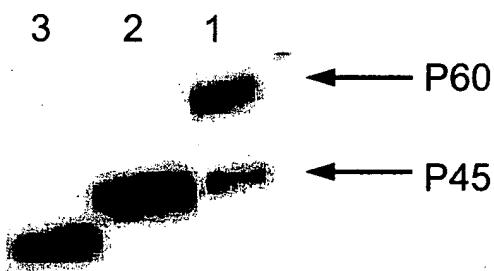
Western blot analysis

Fig. 16

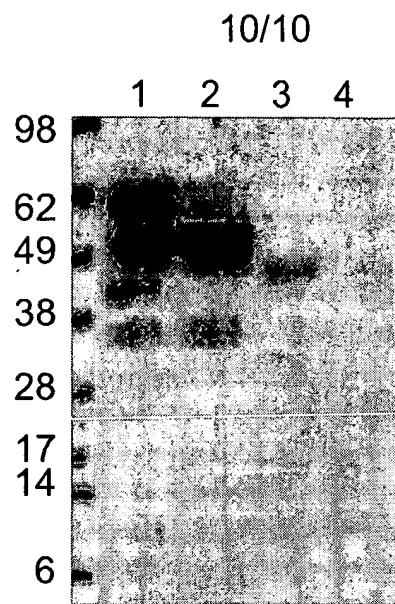


Fig. 17a

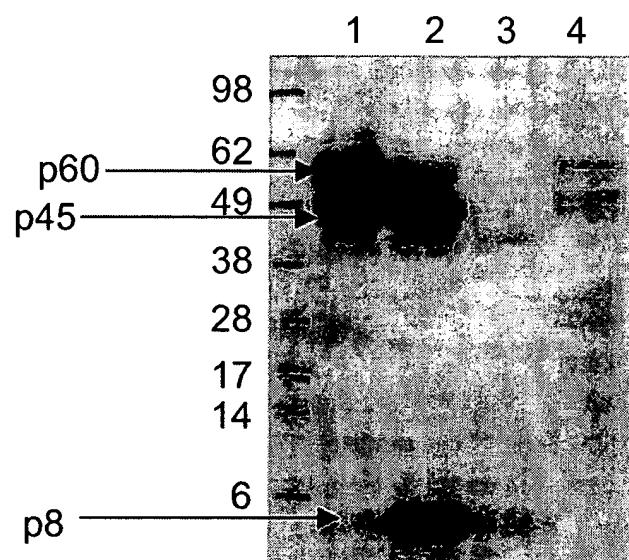


Fig. 17b

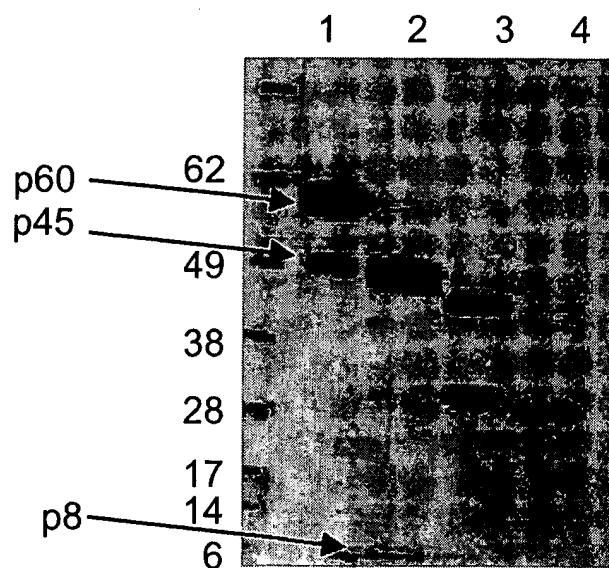


Fig. 17c